

REMARKS

A number of claims were rejected under 35 U.S.C. § 112 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the invention was filed, had possession of the claimed invention. Specifically, the Examiner cited a limitation directed at a "flexible liquid light guide" in which the "instant disclosure as filed failed to include a written basis for this limitation in its broad form" at page 2 paragraph 3 of the Office Action of March 26, 2002.

Accordingly, claims 1, 11, 16, and 29 have been amended to include clarifying language specifically describing the flexible liquid light guide to be formed of a flexible liquid containing member that is capable of mechanically isolating the image capture device from the illumination apparatus. For example, claim 1 has been amended to include the following clarifying language:

"wherein the flexible liquid light guide comprises a flexible member suitably arranged to contain the liquid and capable of vibrationally isolating the image capturing device from the illumination apparatus"

which, as the Examiner has noted, is supported at page 16 lines 1 – 15 of the specification.

Accordingly, the Applicant respectfully requests that the Examiner withdraw the 35 U.S.C. § 112 rejection of claims 1, 11, 16, and 29 and all dependent claims thereof.

A number of claims have been rejected under 35 U.S.C. 103(a) as being unpatentable over Hemstreet in view of Sutherland *et al.* U.S. Patent No. 4,818,710 ("Sutherland"). In addition, the claims been rejected under 35 U.S.C. 103(a) as being unpatentable over Hemstreet in view of Sutherland and in further view of Balch U.S. Patent No. 6,083,763 ("Balch") or *In re Venner* (120 USPQ 193); all being taken in view of Rutenberg *et al.* U.S. Patent No. 5,287,272. This rejection is respectfully traversed.

Hemstreet is cited as teaching a fluorescence imaging system with the capability of digital analysis of the cellular images. Hemstreet is also said to teach image analysis storage and retrieval and the evaluation of the samples for various criteria such as cancer risk assessment. Hemstreet lacks specifics regarding the illumination system that is used in the imaging system. Sutherland is cited as teaching a liquid light guide illumination system for use with microscope slide samples. Balch is said to describe the use of robotic arms for moving samples during

sample preparation during assays. Venner is cited for its holding that automation of a manual method is obvious. Rutenberg is said to describe the use of barcodes on assay items.

As discussed above, the present invention is drawn to a system for capturing images of cells that utilizes a flexible liquid light guide. Other elements of the system include an image capturing device, an image processing device, and database storage device. Other embodiments include an image capturing device, an illumination apparatus, a robotic arm, and software for analyzing the images and characterizing the features.

The shortcomings of Hemstreet have discussed above. Sutherland does not rectify these deficiencies. More specifically, Sutherland teaches the use of a light source 6 with a waveguide 8. See Fig. 2 of Sutherland. The light source is a xenon flash lamp. The analytical cell or cuvette is based on a microscope slide waveguide system. See Sutherland at column 9, lines 18-20. The waveguide 8 is actually the bottom of the microscope slide. See Sutherland at column 9, lines 20-21. An index matching oil is used between the microscope slide and the cuvette 7. Two-quarter round silica prisms 16 and 17 form the sides of the oil reservoir. See Sutherland at column 9, lines 25-27. Thus, the "liquid light guide" taught by Sutherland is an oil-filled reservoir formed by a cuvette, a microscope slide, and two silica prisms.

In contrast to Sutherland, the present specification states at page 16 that the light guide is suitably selected to have a *flexible* member that contains a liquid capable of vibrationally isolating the image capturing device from the illumination apparatus and which also can be used to place lamp source at a remote location away from the imaging device. The flexible member substantially keeps any vibration from the lamp assembly away from the imaging device. In the described embodiments, the light guide is a *flexible* hose-type sleeve filled with a liquid such as an aqueous solution containing chloride or phosphate.

The difference between the flexible liquid light guide of claimed invention and the rigid light guide of Sutherland is further highlighted by the purposes of the two liquid guides. More specifically, the flexible liquid light guide of the instant invention serves to insulate the imaging device from any vibration from the lamp assembly. The purpose of the Sutherland light guide is to eliminate the need for specially polished, optically flat waveguide faces. Applicants submit that a flexible light guide (as used in the instant application) would not accomplish this purpose.

Neither Hemstreet nor Sutherland, either alone or in combination, teach the use of a flexible liquid light guide in an image capturing system. None of the secondary references cure the lack of suggestion of the primary reference(s) to use a flexible liquid light guide in an image capturing system.

For these reasons, withdrawal of the rejections is respectfully requested.

Conclusion

The Applicant respectfully maintains that all pending claims are in condition for allowance. Therefore, the Applicant respectfully requests a Notice of Allowance for this Application from the Examiner. Should any unresolved issues remain, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,
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1. (Amended) A system for capturing images of cells or cell structures, the system comprising:

a cell holder comprising a plurality of sites in a spatial orientation, each of the sites being capable of holding a plurality of cells to be imaged;

an image capturing device coupled to the cell holder, the image capturing device being adapted to capture at least one image in at least one of the plurality of sites;

an illumination apparatus comprising a flexible liquid light guide coupled to the cell holder for highlighting the plurality of sites in a relatively even spatial manner for image capturing purposes, **wherein the flexible liquid light guide comprises a flexible member suitably arranged to contain the liquid and capable of vibrationally isolating the image capturing device from the illumination apparatus;**

an image processing device coupled to the image capturing device, the image capturing device being adapted to convert the image into a digital representation; and

a database storage device comprising a database management element coupled to the image capturing device, the database storage device being adapted to retrieve the digital representation of the image from the image processing device and storing the digital representation.

11. (Amended) A database system comprising:

a plate comprising a plurality of sites in a spatial orientation, each of the sites being capable of holding a plurality of cells to be imaged;

a light source comprising a flexible liquid light guide coupled to the plate for illuminating the plurality of cells in a relatively uniform spatial manner for image capture purposes;

an image capturing device to capture a plurality of images of at least one of the sites, the image capturing device coupled to the plate, **wherein the flexible liquid light guide comprises a flexible member suitably arranged to contain the liquid and capable of vibrationally isolating the image capturing device from the light source;**

an image processing device to combine a first image and a second image from the plurality of images, the image processing device coupled to the image capturing device, the image processing device being adapted to form a plurality of respective features of the plurality of images; and

a database storage device comprising a database management element coupled to the image processing device, the database storage device being adapted to retrieve the plurality of features and store the plurality of features.

16. (Amended) A system for capturing cellular information from a population of cells, the system comprising:

an image acquisition system comprising a charged coupled camera adapted to capture an image of a plurality of manipulated cells, the illumination apparatus providing for an acquisition of the image of the plurality of manipulated cells;

an illumination apparatus comprising a flexible liquid light guide coupled to the image acquisition system for highlighting the plurality of manipulated cells, **wherein the flexible liquid light guide comprises a flexible member suitably arranged to contain the liquid and capable of vibrationally isolating the image acquisition system from the illumination apparatus;** and

a database system coupled to the image acquisition system, the database system being adapted to be populated with information of the image of the plurality of manipulated cells;

wherein the information comprises a plurality of descriptors, each of the descriptors comprising a plurality of features, each of the features corresponding to a cellular or subcellular component from the plurality of manipulated cells.

29. (Amended) A system for capturing images of cells or cell structures from multiple cell holders, each comprising a plurality of sites in a spatial orientation, each of the sites being capable of holding a plurality of cells to be imaged, the system comprising:

an image capturing device coupled to the cell holder, the image capturing device being adapted to capture at least one image in at least one of the plurality of sites;

an illumination apparatus comprising a flexible liquid light guide coupled to the cell holder for highlighting the plurality of cells in a relatively even spatial manner for image capturing purposes, **wherein the flexible liquid light guide comprises a flexible member suitably arranged to contain the liquid and capable of vibrationally isolating the image capturing device from the illumination apparatus;**

a robot arm for automatically collecting multiple of said cell holders to facilitate capture of the images of the cells or cell structures from said multiple cell holders; and

software that analyzes the images and characterizing features of the cells or cell structures in the images.